UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,425	03/03/2005	Tsuneko Okazaki	80161(302730)	9673

21874 7590 10/15/2009

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
HILL, KEVIN KAI	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
10/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,425	OKAZAKI ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,14,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,14,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on October 1, 2007 is acknowledged.

Applicant has elected with traverse the invention of Group I, claim(s) 1, 3-7 and 13-14, drawn to a method of producing a circular mammalian artificial chromosome.

Within Group I, Applicant has elected the insertion sequence species "lox P site", as recited in Claim 13.

Amendments

Applicant's response and amendments, filed August 3, 2009, to the prior Office Action is acknowledged. Applicant has cancelled Claims 2-3, 5-6, 8-13 and 15-56, amended Claim 1, and added new claims, Claims 57-58.

Claims 1, 4, 7, 14 and 57-58 are under consideration.

Priority

This application is a 371 of PCT/JP03/11134, filed September 1, 2003. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Certified copies of the foreign patent applications Japan 2002-258114, filed September 3, 2002 and Japan 2002-338865, filed November 22, 2002 are filed with the instant application. Certified English translations of said foreign applications have not been provided.

Examiner's Note

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the August 3, 2009 response will be addressed to the extent that they apply to current rejection(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

1 **The prior rejection of Claims 1, 4-7 and 13-14 under 35 U.S.C. 112, second paragraph, is withdrawn** in light of Applicant's amendment to the claim to recite that the second vector is introduced into the same mammalian host cell as the first vector.

Claim Rejections - 35 USC § 103

2. **Claims 1 and 4 stand, and Claim 57 is newly rejected under 35 U.S.C. 103(a)** as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in view of Perkins et al (US 2003/0119104 A1), Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986) and Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE).

Response to Arguments

Applicant argues that the disclosure on in [0146] and Example 1 where a 21-I alphoid fragment is used, where a preference for an alpha satellite region from human chromosome 21 is taught and is *shown not to be a functional equivalent:* It is preferably to use a sequence derived from an alpha satellite region of a human chromosome 21. The alpha satellite region of the human chromosome 21 has been investigated in detail and has a region called a21-I. The a21-I region includes a sequence called an alphoid 11-mer repeat unit. This repeat unit includes a plurality of CENP-B boxes consisting of 5'-NTTCGTTGGAAACGGGA-3' (SEQ ID NO: 2) at regular intervals (Ikeno et al. Human Mol. Genet., 3, 1245-1247, 1994).

Applicant's arguments have been fully considered, but are unpersuasive. The cited portion of the specification simply discloses the preference for an alpha satellite region of a human chromosome 21, more specifically α21-I. However, said disclosure does NOT show α21-I to not be a functional equivalent. Ikeno et al teach that the alpha satellite region of a human chromosome 21, more specifically α21-I, is involved in common centromere function.

Furthermore, Ikeno et al clearly teach the CENP-B box to comprise SEQ ID NO:2 (Table 1; pg 1254).

3. **Claim 7 stands rejected under 35 U.S.C. 103(a)** as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE) and Perkins et al (US 2003/0119104 A1), as applied to claims 1, 4 and 57 above, and in further view of Bokkelen et al (U.S. Patent No. 5,695,967).

4. **Claim 14 stands rejected under 35 U.S.C. 103(a)** as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE), Perkins et al (US 2003/0119104 A1) and Bokkelen et al (U.S. Patent No. 5,695,967), as applied to claims 1, 4, 7 and 57 above, and in further view of Cooke et al (WO 00/18941).

Response to Arguments

Applicant argues that no combination of Mejia with any of the secondary references cited expressly or inherently teaches the invention as claimed. None of the Waye et al., Ikeno et al., Perkins et. al. Bokkelen or Cooke et al. references cures the defects of the Mejia reference and teaches a mammalian centromere sequence as claimed.

Applicant's arguments have been fully considered, but are unpersuasive. Applicant is respectfully reminded that at the time of the invention, α satellite (alphoid) DNA was known in the prior art to form a functional centromere in a human artificial chromosome, wherein the presence of a centromere protein B sequence (CENP-B box) in the alphoid DNA is a requirement for the functional centromere. Waye et al taught the sequence of the human chromosome 17 centromere comprising nucleic acid sequences 100% identical to SEQ ID NO:1. Furthermore, Ikeno et al taught a consensus CENP-B box nucleotide sequence from human chromosome 21 alphoid repeats, wherein the human chromosome 17 centromere comprises an 11-mer repeat with 100% identity to the consensus sequence set forth by Ikeno et al.

Absent evidence to the contrary, nothing non-obvious is seen with substituting a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 17 with a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 21 because both such centromere sequences comprise an 11-mer repeat with 100% identity to the consensus sequence set forth by Ikeno et al of the consensus CENP-B box nucleotide sequence, and thus are considered functional equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). See MPEP §2144.06

5. **Claim 58 is rejected under 35 U.S.C. 103(a)** as being unpatentable over Mejia et al (Genomics 70(2):165-170, 2000; *of record in IDS, AE), in further view of Waye et al (Mol. and Cell. Biol. 6(9):3156-3165, 1986), Ikeno et al (Human Mol. Gen. 3(8):1245-1257, 1994; *of record in IDS, CE), Perkins et al (US 2003/0119104 A1), Bokkelen et al (U.S. Patent No.

5,695,967) and Cooke et al (WO 00/18941), as applied to claims 1, 4, 7, 14 and 57 above, and in further view of Okazaki et al (WO 98/08964).

The prior cited art does not teach a mammalian centromere sequence obtained from human chromosome 21 to comprise a sequence of SEQ ID NO:3. However, at the time of the invention, Applicant's own work (Okazaki et al) disclosed mammalian artificial chromosomes comprising a centromere obtained from human chromosome 21, wherein said centromere comprises a sequence 100% identical to SEQ ID NO:3 (search results available in SCORE).

It would have been obvious to one of ordinary skill in the art to substitute a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 17 with a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 21 comprising SEQ ID NO:3 with a reasonable expectation of success because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)". When substituting equivalents known in the prior art for the same purpose, an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). M.P.E.P. §2144.06. An artisan would be motivated to substitute a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 17 with a mammalian centromere sequence comprising an 11mer repeat unit obtained from human chromosome 21 comprising SEQ ID NO:3 because Applicant's own prior work successfully demonstrated a method of producing a mammalian artificial chromosome comprising a centromere obtained from human chromosome 21 comprising SEQ ID NO:3 and teach that the nucleic acid has sufficient quantity of CENP-B box spaced repeats to provide centromere properties to a DNA construct in a host cell.

The cited prior art meets the criteria set forth in both *Graham* and *KSR*, and the teachings of the cited prior art provide the requisite teachings and motivations with a clear, reasonable expectation of success. Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

Conclusion

6. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kevin K. Hill

Examiner, Art Unit 1633

/Anne Marie S. Wehbe/
Primary Examiner, Art Unit 1633